CHAPTER 1

INTRODUCTION

1.1 Biodegradable Polymers

Biodegradable polymers, especially aliphatic polyesters, have been investigated worldwide as biomaterials for medical, pharmaceutical and industrial applications due to their biocompatibility and biodegradability. [1-2] The term "biodegradable" refers to degradation induced by the vital activity of an organism, not simply the degradation of a material in a physiological environment. However, the term "biodegradable polymer" is now widely used to convey the meaning of a polymer that degrades in the human body. [3] The generally accepted definition of "polymer biodegradation" is; hydrolytic, enzymatic or bacteriological degradation processes occurring in a polymer which do not necessarily proceed to a stage where the physical form of the polymer is altered. [4] Consequently, the design of biodegradable polymers with tailored properties has become one of the most challenging problems for polymer scientists. A basic prerequisite for medical applications is the absolute biocompatibility of the polymers and their degradation products. [5]

Aliphatic polyesters such as polylactide, PLL, poly(glycolic acid), PGA, and poly(ε-caprolactone), PCL, are widely used in medical applications because they can control the equilibrium of their properties. In the theory, ester group will be hydrolysable, hydrophilicity, degradable and absorbable, methylene group and ether group in the polymer structure will increase the main chain flexible. Their great

advantage is their degradability by simple hydrolysis of the ester bond in aqueous environment such as body fluids. Furthermore, the degradation products are ultimately metabolized *in vivo* to carbon dioxide and water or are excreted *via* the kidney. [6] In general, synthetic polymers offer greater advantages than natural materials in that they can be tailored to give a wider range of properties and more predictable uniformity than materials from natural sources. Some examples of biodegradable polyesters currently used in medicine are listed in Table 1.1.

Table 1.1 Some biodegradable polymers used in medicine. [7]

Application	Trade Name	Composition	Manufacturer
Sutures	Dexon	PGA	Davis and Geck
	Maxon	PGA-TMC	Davis and Geck
	Vicryl	PGA-LPLA	Ethicon
	Monocryl	PGA-PCL	Ethicon
	PDS	PDO	Ethicon
	Polysorb	PGA-LPLA	U.S. Surgical
	Biosyn	PDO-PGA-TMC	U.S. Surgical
	PGA Suture	PGA	Lukens
Interference screws	Sysorb	DLPLA	Synos
	Endofix	PGA-TMC or LPLA	Acufex
	Arthrex	LPLA	Arthrex
	Bioscrew	LPLA	Linvatec
	Phusiline	LPLA-DLPLA	Phusis
	Biologically Quiet	PGA-DLPLA	Instrument Makar
Suture anchor	Bio-Statak	LPLA	Zimmer
	Suretac	PGA-TMC	Acufex
Anastomosis clip	Lactasorb	LPLA	Davis and Geck
Anastomosis ring	Valtrac	PGA	Davis and Geck
Dental	Drilac	DLPLA	THM Biomedical

Table 1.1 Continued

Application	Trade Name	Composition	Manufacturer
Angioplastic plug	Angioseal	PGA-DLPLA	AHP
Screw	SmartScrew	LPLA	Bionx
Pins and rods	Biofix	LPLA or PGA	Bionx
	Resor-Pin	LPLA-DLPLA	Geistlich
Tack	SmartTack	LPLA	Bionx
Plates, mesh, screws	LactoSorb	PGA-LPLA	Lorenz
Guided tissue	Antrisorb	DLPLA	Atrix
	Resolut	PGA-DLPLA	W.L. Gore
	Guidor	DLPLA	Procordia

1.2 Absorbable Nerve Guides

Many new applications are being developed for the use of biodegradable polymers in tissue regeneration. Nerves are one of the first tissues for which the method of guided tissue regeneration has been tried. The most severe form of peripheral nerve damage is a total lesion and consequential loss of nerve function. Although peripheral nerves can regenerate spontaneously, their function is not automatically restored. Direct reconnection by suturing of the proximal and distal nerve stumps is the first choice in the repair of a nerve gap as shown in Figure 1.1(a). However, tension at the suture site is a very unfavorable factor. Transplantation of autologous nerve grafts is now a standard method when the nerve gap is large as shown in Figure 1.1 (b). The donor nerve is usually obtained from nerves which are functionally less important such as the sural nerve and superficial cutaneous nerves. The results of nerve grafts are not entirely satisfactory either because of the limited availability of donor nerves, morbidity at the donor site, mismatch between nerve and grafts and additional operation time. [8-9] Both techniques are time-consuming, give

rise to complication and do not lead to optimal nerve function recovery. Artificial nerve guides, where a tube bridges the nerve gap, offer a promising alternative to peripheral nerve repair as shown in Figure 1.1(c). Polymeric conduits, both biodurable and biodegradable, have been used. Biodurable nerve conduits constructed of silicone rubber, acrylic polymer and polyethylene have the disadvantage that they remain in the body, provoking a continuous inflammatory response, such that a second operation might be necessary to remove them which may lead to injury to the regenerated nerve. [8]

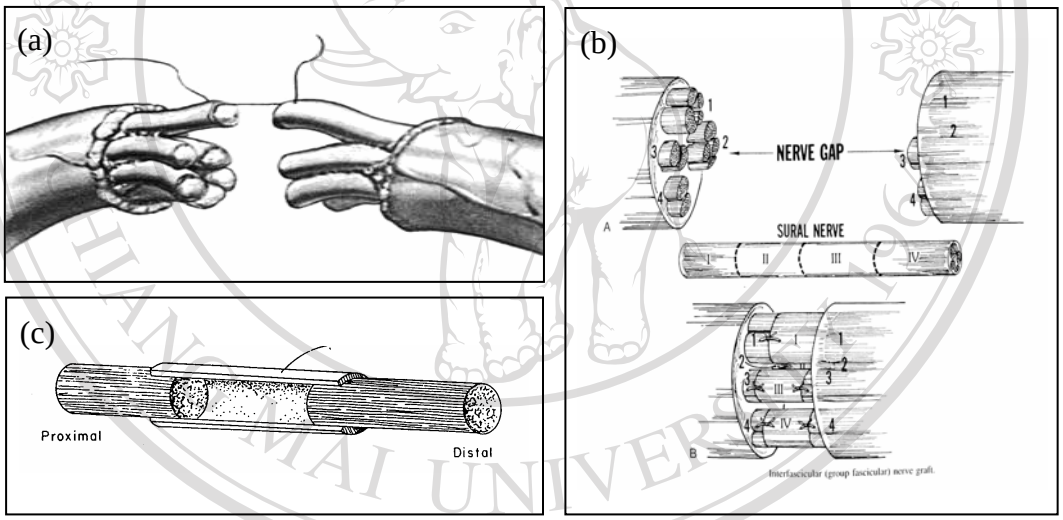


Figure 1.1 Nerve repair methods (a) nerve suture (b) nerve graft and (c) nerve guide.

Various types of biodegradable nerve conduits have been developed. [10-12] The idea behind the use of a biodegradable nerve conduit is that the nerve guide directs the outgrowing nerve fibers towards the distal nerve stump, while preventing neuroma formation and in growth of fibrous tissue into the nerve gap. After the nerve function has been restored, the nerve guide is gradually degraded without inducing scar tissue formation. The rate of biodegradation of nerve guides should be in

accordance with axonal growth rates, and researchers are still developing new types of biodegradable nerve conduits. [8] The conduits may be implanted empty or filled with growth factors, cells or fibers. A nerve guide should have an internal diameter large enough to overcome problems when telescoping the nerve stumps into the lumen of the nerve during the implantation procedure. It should also have a thin wall that swells minimally during degradation and causes no nerve compression.

The absorbable nerve guide should be flexible, but relatively strong and easy to handle in microsurgery. In order to bridge large nerve defects in clinically relevant situations, it is anticipated that a suitable period is required for the nerve to regenerate and maturate. In previous studies, promising results have been obtained with polyglycolic acid, poly(organo)phosphazene and poly(L-lactide-*co*-ε-caprolactone) conduits. [10-12] Neurotube® (Neurogen LLC,USA) and Neurolac® (Polyganics BV, The Netherlands) have been approved by the American Food and Drug Administration (FDA) as commercial bioabsorbable nerve conduits made from polyglycolic acid and poly(L-lactide-*co*-ε-caprolactone) respectively. A randomized prospective clinical trail comparing a biodegradable polyglycolic acid conduit with standard end-to-end and nerve graft repairs was carried out. [10] Polyglycolic acid conduit repair gave results superior to those of a nerve graft for longer nerve gaps and eliminated the donor-site morbidity associated with nerve graft harvesting. [10] Meek and Coert [8] reviewed the clinical use of nerve conduits in peripheral nerve repair, concluding that so far only the biodegradable polyglycolic acid conduits have proved their value in the clinical reconstruction of nerve defects. The availability of conduits with material properties appropriate for nerve regeneration will continue to increase

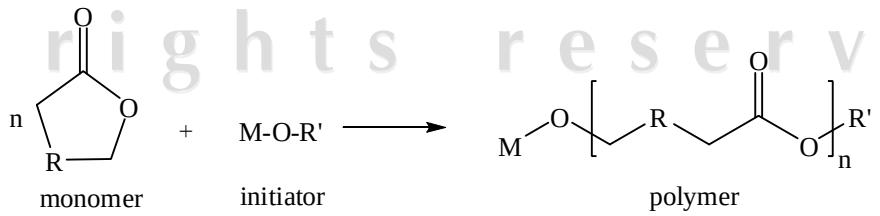
as new biodegradable polymers and processing conditions are developed and approved for clinical use. [13]

In Biomedical Polymers Technology Unit, Department of Chemistry, Faculty of Science, Chiang Mai University the possibility of using novel polyesters based on L-lactide, ε-caprolactone and glycolide for use as absorbable nerve guide is being studied. [14]

1.3 Ring-Opening Polymerization of Cyclic Esters

Aliphatic polyesters can be synthesized through either polycondensation of acids and alcohols or ring-opening polymerization (ROP) of cyclic esters. In contrast to the traditional step-polycondensation method, the ROP of a cyclic ester is an effective method of preparation of aliphatic polyester. Under rather mild conditions, high molecular weight aliphatic polyesters can be prepared in short periods of time. [15] The development of ROP of lactones, anhydrides and carbonates started around 1930. [16-17]

Aliphatic polyesters of high molecular weight are exclusively produced by the ROP of the corresponding cyclic monomers. Polyester is formed when cyclic esters are related with a catalyst or initiator. Scheme 1.1 presents the reaction pathway for the ROP of a cyclic ester.



Scheme 1.1 Representation of the ROP of a cyclic ester: R=$(CH_2)_{0-3}$ and/or (CHR″).

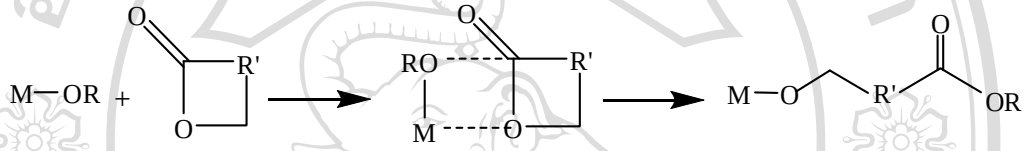
Each macromolecule formed will generally contains one chain end terminated with a functional group originating from the termination reaction and one terminus end-capped with a functional group originating from initiator. By altering the initiator and the termination reaction, the nature of the functional groups can be variety to fit the application of the polymer. The types of initiator and end-group play important roles in determining both the thermal stability of the resulting polyester. [18-19] Functional groups accessible to post-polymerization reactions can also be introduced into the polymer structure in this way.

The ROP reaction can be performed either as a bulk polymerization or in solution, emulsion, or dispersion. [20-21] A catalyst or initiator is necessary to start the polymerization. Under mild conditions, high molecular weight aliphatic polyesters of low polydispersity can be prepared in short periods of time. Problems associated with condensation polymerization, such as the need of exact stoichiometry, high reaction temperature, and the removal of low molecular weight by-products (*e.g.*, water) are excluded in ROP. Depend on the initiator, the polymerization proceeds according to one of three different major reaction mechanisms [22], *viz*., cationic, anionic, or coordination-insertion mechanisms. [23-24] In addition, radical, switterionic and active hydrogen [22] initiation is also possible, although such techniques are not used to any great extent. The focus in this section is on the "coordination-insertion" mechanism.

1.4 Coordination-Insertion Ring-Opening Polymerization

The pseudo-anionic ROP is often referred to as coordination-insertion ROP, since the propagation is thought to proceed by coordination of the monomer to the

active species, followed by insertion of the monomer into the metal-oxygen bond by rearrangement of the electrons. [23] Scheme 1.2 shows a schematic presentation of the coordination-insertion mechanism. The growing chain remains attached to the metal through an alkoxide bond during the propagation. The reaction is terminated by hydrolysis forming a hydroxyl end group. With functional alkoxy-substituted initiators, macromers with end groups active in post-polymerization reactions are produced.



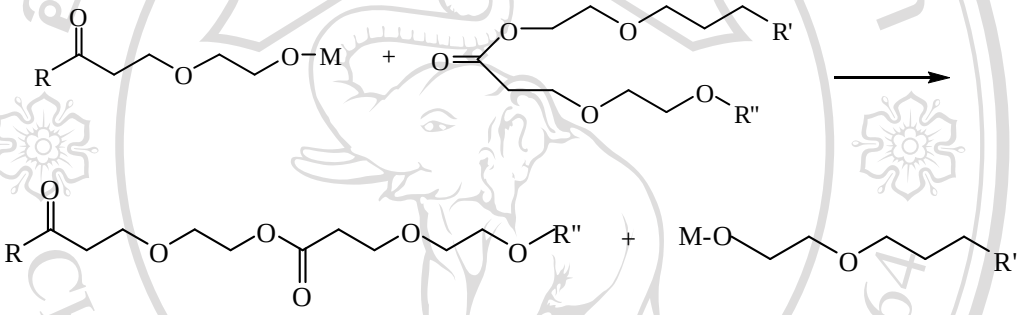
Scheme 1.2 The reaction pathway for the ROP of a cyclic ester by the coordination-insertion mechanism.

1.5 Transesterification Reactions

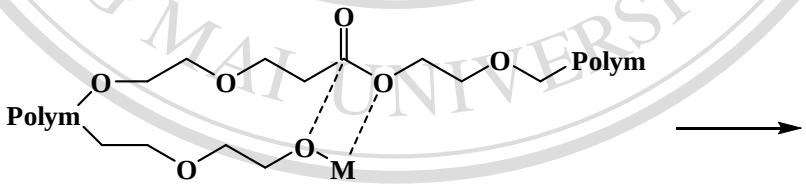
The ROP of cyclic esters with these organometallic initiators at high temperature or long reaction times leads to both inter- and intramolecular transesterification reactions. Both types of transesterification reaction lead to increase in molecular weight distribution of the polyesters. As shown in Scheme 1.3, each intramolecular transesterification randomly breaks the polymer chain. In this way, an attack on the polymer chain leads to a free residual polymer and new randomized, modified polymer. According to this, an original copolymer with a block like-structure would be converted to a randomized copolymer after undergoing transesterification. [15] The reaction parameters that influence the number of transesterification are reaction temperature, reaction time, type and concentration of

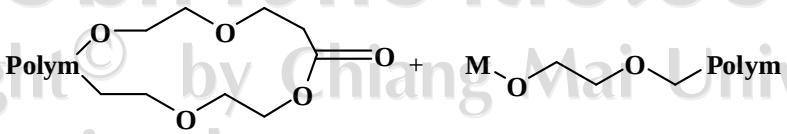
catalyst or initiator. Depending on the metal used, the initiator is more or less active towards side-reactions such as transesterification reactions. [25] Grijpma *et al.* [26-27] studied the effects of the reaction temperature and the reaction time and demonstrated the increasing importance of transesterification reaction with temperatures.

Intermolecular Transesterification



Intramolecular Transesterification (Back-biting)

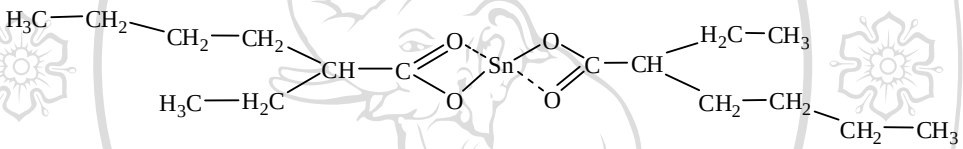




Scheme 1.3 Reaction schemes for intermolecular and intramolecular transesterification reactions.

1.6 Tin(II) 2-Ethylhexanoate

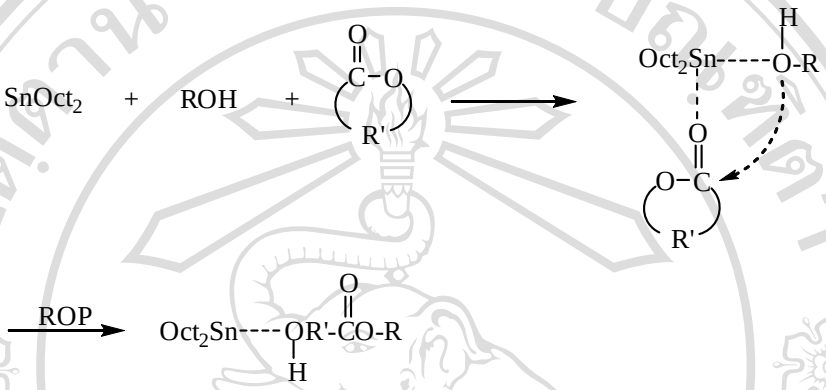
The most widely used catalyst for coordination-insertion polymerization of aliphatic polyesters is tin(II) 2-ethylhexanoate. It is also known as stannous octoate ($SnOct_2$) in the industry and exists in the form as shown in Scheme 1.4. It is a very effective and versatile catalyst, which is easy to handle and is soluble in common organic solvents and cyclic ester monomers. The FDA has approved it is a food additive. [26-30]



Scheme 1.4 Tin(II) 2-ethylhexanoate or stannous octoate ($SnOct_2$).

The $SnOct_2$ is not thought to be the actual initiator since the molecular weight does not depend on the monomer to $SnOct_2$ molar ratio. The most promising mechanism is a coordination-insertion mechanism where a hydroxyl functional group is thought to coordinate to $SnOct_2$, forming the initiating tin alkoxide complex. Investigations of the coordination-insertion mechanism have resulted in two slightly different reaction pathways. Recently, the generally accepted "coordination-insertion" mechanism for $SnOct_2$ catalyzed ROP of lactones and lactides has been demonstrated by Kricheldorf *et al.* [31, 33] and Penczek *et al.* [32, 34-35] although there are still some debates.

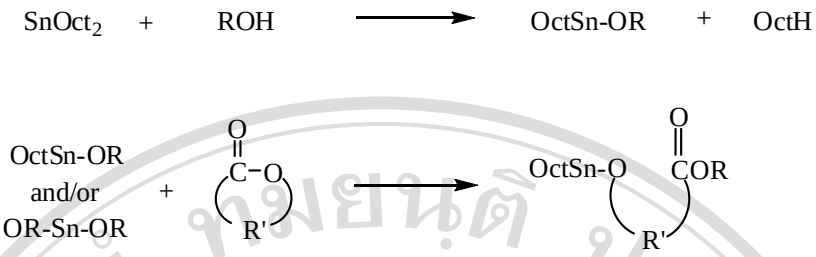
Kricheldorf *et al.* [31, 33] have proposed a mechanism where the initiating alcohol functionality and the monomer are both coordinated to the complex during propagation. The reaction is terminated by hydrolysis forming a hydroxyl end group in Scheme 1.5.



Scheme 1.5 The main ROP mechanism proposals with $SnOct_2$ as catalyst that the complexation of a monomer and alcohol prior to ROP.

Penczek *et al.* [32, 34-35] proposed the alternative mechanism suggesting that when $SnOct_2$ mixed with an alcohol an initiating complex is formed prior to polymerization. The establishment of equilibrium between $SnOct_2$ and alcohol results in the liberation of acid from the catalyst. The tin alkoxide complex thus formed then initiates the polymerization. The presence of tin alkoxide complex has recently been reported by using MALDI-TOF spectroscopy for both lactide [34] and ε-caprolactone [35] polymerization. Scheme 1.6 shows the $SnOct_2$ catalyst is a strong transesterification agent, and the resulting copolymers normally have a randomized microstructure. [36]

It is now widely accepted that the $SnOct_2$ and ROH react together *in situ* to form the corresponding tin(II) alkoxide, which are the true initiator.

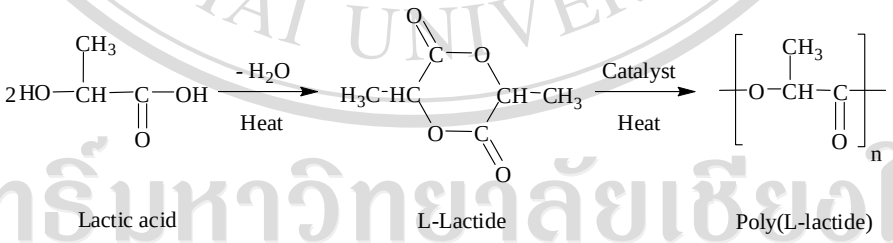


Scheme 1.6 The main ROP mechanism proposals with $SnOct_2$ as catalyst that the formation of a tin alkoxide before ROP.

1.7 Poly(L-lactide) (PLL)

1.7.1 Polymer Synthesis

Although lactic acid can be polymerized directly to poly(lactic acid), a much higher polymer molecular weight is achieved by first converting the lactic acid to lactide. Hence, the polymer is commonly known as poly(L-lactide) (PLL). The sequence of reactions is shown in Scheme 1.7.



Scheme 1.7 Conversion of lactic acid into high molecular weight polylactide requires the preparation of high-purity lactide as the monomer intermediate. [37]

In the bulk polymerization of lactides, temperatures in the range of 105-185°C for L-lactide and D-lactide and 135-155°C for DL-lactide are typical, although lower

temperatures can be used. When polymerization temperatures are less than the T_m of the poly(L-lactide) and poly(D-lactide) (~ 175°C), crystallization of the polymerizing polymer occurs resulting in what is known as solid-state polymerization. Solid-state polymerization can be a useful tool in forming very high molecular weight polymers ($\overline{M}_n$ ~1,000,000). The polylactide polymerization reaction is typically initiated by $SnOct_2$ because of its very low toxicity. Other initiators which can be used include various Lewis acids, organometallic compounds and organic acids.

1.7.2 Polymer Properties [38]

Poly(L-lactide) (PLL) is a crystalline, biodegradable polymer having a melting point (T_m) of approximately 175°C and a glass transition temperature (T_g) of approximately 65°C. The calculated value for the heat of fusion of 100% crystalline polymer has been reported as 93.7 J/g with a specific gravity of approximately 1.2-1.3. In contrast, poly(DL-lactide) (PDLL) is a completely amorphous polymer having a T_g of approximately 57°C. Its specific gravity is approximately 1.2-1.3, similar to PLL. All types of polylactides are soluble in most organic solvents.

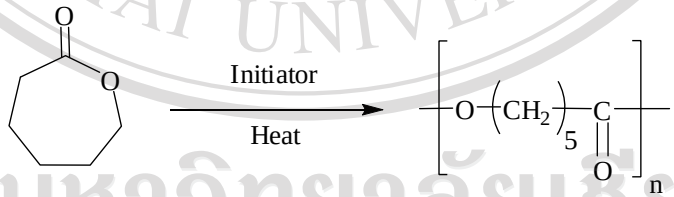
Metabolically almost all of the amino acids that occur naturally in proteins have the L-configuration. Likewise, only L-lactic acid is produced in muscle tissue during vigorous exercise (anaerobic glycolysis). Excess lactic acid which accumulates in the blood is later recycled by conversion to glycogen in the liver. This metabolic pathway begins with the transformation of lactate to private by enzyme lactate dehydrogenate which only accepts L-lactic acid. Any D-lactic acid present in

the blood stream as a result of the hydrolysis of a poly(D-lactide) implant would be excluded from this pathway and presumably excreted unchanged.

1.8 Poly(*ε*-caprolactone) (PCL)

1.8.1 Polymer Synthesis

Poly(*ε*-caprolactone) (PCL) provides another example of a bioabsorbable polyester prepared by the ROP of a cyclic ester monomer. In this case, the monomer is *ε*-caprolactone, a seven-membered ring in which a single ester moiety is linked together with five methylene group units. The ROP temperatures for PCL are in the range of 140-150°C with the polymerization again being normally initiated by $SnOct_2$. Other initiators which have been used include various Lewis acids, metal alkyls and organic acids. Molecular weight is controlled by the addition of chain control agents. These chain control agents are usually water, primary alcohols, amines, or some other active hydrogen compound.



CL PCL

1.8.2 Polymer Properties [38]

PCL is a hydrophobic, semi-crystalline polymer having a low T_m ~ 60°C and a T_g ~ -60°C. The repeating molecular structure of PCL consists of five nonpolar methylene groups and a single relatively polar ester group. This structure gives PCL

some unique properties. The mechanical properties are similar to polyolefins because of its high olefinic content, while the presence of the hydrolytically unstable aliphatic ester linkage causes the polymer to be biodegradable. PCL is degraded very slowly *in vivo*, initiated by non-enzymatic ester hydrolysis of its backbone ester bonds to yield ε-hydroxycaproic acid, which enters the citric acid cycle and is completely metabolized.

1.9 Previous Work Relevant to This Study

In recent years, design and synthesis of biodegradable polymers have attracted interest and efforts of scientists engaged in biomaterial design. Aliphatic polyesters, prepared by ring-opening polymerization of lactones and lactide, are versatile polymers having good mechanical properties, hydrolyzability and biocompatibility. These attributes make them a leading candidate in biomedical and pharmaceutical industries as a resorbable implant material and a vehicle for controlled drug delivery. Earlier studies on aliphatic homopolyesters and copolyesters in the 1960s were aimed at developing materials for surgical implants and tissue repair. [39-41]

The polyesters of biomedical importance are derived from glycolide (G), lactide (LL) and ε-caprolactone (CL). Previous studies of the synthesis of copolymer, for example, copolymer of lactide and glycolide [42-43], lactide and ε-caprolactone [26, 44-45], glycolide and ε-caprolactone [46-47] and also random copolymer, block copolymer and terpolymer [44, 48-50] revealed about controlled structure and properties of polymers and studies about the influence of the condition used such as reaction temperature, reaction time, type of initiator/co-initiator on polymer properties. [15, 26, 44-48] Most applications require high molecular weight polymers and the

preferred route for the synthesis polymer is bulk ROP in the presence of $SnOct_2$ as a catalyst and alcohol as an initiator. Many previous works indicate that the molecular weight and the molecular weight distributions of aliphatic polyesters can be controlled with very dry system, high purities and with a controlled amount of a hydroxyl-containing compound used. [33, 51-52]

Whereas the literature contains sufficient information on the choice of suitable reaction parameters for bulk polymerization in a small-scale reaction, the prior art contains no teaching as to how the reaction can be carried out on an industrial scale. [53] Amongst the reaction variables which need to carefully control in the bulk ROP of cyclic esters are:

(a) **Reaction temperature, reaction time and concentrations of initiator** have a great influence on the reaction rate, % conversion, molecular weight and on the nature of the polymer product formed. The profile of monomer conversion with time at different temperatures shows that an increase in reaction temperature and time usually results in an expected acceleration of polymerization and in an increase in molecular weight. However, the longer reaction temperature and reaction time leading to the transesterification reaction. The intermolecular transesterification reaction leading to the sequence of the monomer. While, the intramolecular transesterification reaction such as back-biting leading to cyclic oligomer. So, the polymer has the broad molecular weight distribution. The previous related studied are briefly shown below.

Kowalski *et al.* [34,52] studied the kinetics of L-lactide polymerization, initiated with tin(II) butoxide ($Sn(OBu)_2$) and carried out in bulk at 120°C. It was

found that the number-average molecular weight ($\overline{M}_n$) of the resulting poly(L-lactide) can be controlled in a wide range of values from 10^3 to 10^6 by adjusting the monomer to initiator molar ratio ($[LA]_0$ / $[Sn(OBu)_2]_0$). Moreover, the monomer conversion increases with the increasing of reaction time.

Finne *et al.* [54] studied the effect of the reaction time on the monomer conversion. It was found that the number-average molecular weight ($\overline{M}_n$) of the polymer obtained increases linearly with the conversion and that the molecular weight distribution was extremely narrow. The molecular weight can be controlled by the monomer to initiator ratio.

Köhn *et al.* [55] and Yuan *et al.* [56] studied the effects of the monomer to initiator ([M]: [I]) molar ratio, reaction temperature and reaction time on the polymer properties. The results show that the yield and molecular weight of the resulting polymer increased with the reaction temperature and time at the initial stage and reached the maximum values, then followed by a rapid decrease at long reaction temperature and reaction time due to transesterification reaction. Furthermore, the yield of polymer increases with the decrease in the [M]: [I] ratio, but the molecular weight of polymer increases with the increase in the [M]: [I]. This is due to the higher concentration of initiator, which increases the number of active species, leading to high conversion of monomer.

Winita *et al.* [14] studied the influence of the polymerization conditions such as reaction temperature, reaction time and concentration of initiator on the poly(L-lactide-*co*-*ε*-caprolactone-*co*-glycolide) 45: 45: 10 mole% terpolymer properties for use as absorbable nerve guide in 7 g using 0.1 mole% of $SnOct_2$ as a catalyst and 0.2 mole% of 1-hexanol as an initiator *via* bulk ROP. The effect of the reaction

temperature (100, 110, 120, 140°C), it was found that rise of reaction temperature caused higher yield of polymer. However, at higher reaction temperature (140°C) and longer reaction time, the transesterification reaction occur leading to low molecular weight of polymer. Furthermore, the concentration of 1-hexanol can controlled the molecular weight of terpolymer.

(b) **Purity of the reactants** is a basic prerequisite to achieve a high degree of polymerization. The reagents should not contain any impurities that initiate additional chains or hinder the build up of chains by forming non-reactive end-groups.

(c) **Method of mixing the monomer and the initiator;** there are two methods for doing this. In the first method, the monomer and the initiator are mixed together at room temperature before heating to the polymerization temperature. This contrasts with the second approach in which the monomer is pre-heated by itself up to the polymerization temperature and initiator then injected rapidly with efficient stirring. It is often found in practice that these different methods lead to differences in % conversion and molecular weight distribution. It may also have an effect on the monomer sequence distribution in random copolymers. In copolymerization sequential monomer addition is another procedural variation.

(d) **Thermodynamics;** The single most important factor that determines whether a cyclic monomer can be converted to linear polymer is the thermodynamic factor, that is, the relative stabilities of the cyclic monomer and linear polymer structure. Equilibrium reactions are controlled by thermodynamics. The standard Gibbs free energy**,** $\Delta G°$, of polymerization is given by the

standard polymerization enthalpy, $\Delta H°$, the temperature, T, the standard polymerization entropy, $\Delta S°$, and the equilibrium constant, K_n, respectively:

$$\Delta G° = \Delta H° - T\Delta S° = -RT \ln K_n \quad \text{at constant pressure, P}$$

As in the case of each polymerization, the free-energy change, $\Delta G°$, should be negative under given reaction conditions. [57-58]

Furthermore, Buchholz *et al.* [53] and Van Der Wal *et al.* [59] studied a process which can be used on an industrial scale for preparing reabsorbable polyesters by bulk polymerization at moderate temperatures by which high molecular weight polyesters can be produced. A preferred process comprises the following steps:

(a) melting the monomer(s) in a stirred reactor (5-10000 liters) and adding the catalyst and a chain length moderator ;

(b) homogenizing the reaction mixture using a stirrer ;

(c) transferring the reaction mixture into smaller plastic containers (0.5-5 liters) through a system of tubes ;

(d) carrying out the polymerization reaction in the plastic containers until the desired degree of reaction of the polymerization is achieved ;

(e) removing the polymer block formed from the plastic containers.

The reactions are preferably carried out isothermically. In some cases, however, it is advantageous to start at lower temperature in order to avoid strongly exothermic reactions, and to raise the temperature as the reaction proceeds in order to increase the speed of reaction of the monomers.

The catalysts are preferably used in low concentrations in order, on the one hand, to minimize the development of heat during the polymerization by keeping the

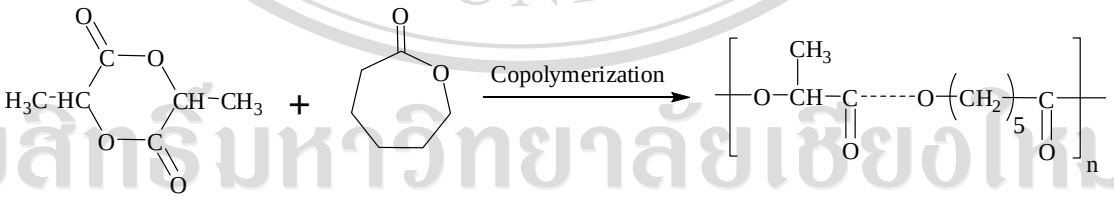
reaction speed low and, on the other hand, to prevent the reaction mass from polymerizing to any appreciable extent while it is still in the melt reaction, which would make the transfer into the plastic containers more difficult because of an increasing of viscosity.

The preferred concentration of the chain length moderator depends on the structure of the moderator and the desired molecular weight of the polymer.

The reaction times required depend on the reactivity of the monomer or monomers, the reaction temperature and the concentration of catalyst and the required degree of conversion.

1.10 Aims of This Study

The main aim of this research project is concerned with the synthesis of biodegradable copolyesters and studies the influence of synthesis scale on the reaction profile in the bulk copolymerization. The aliphatic polyesters of particular interest are copolymers of L-lactide and *ε*-caprolactone, as shown below.



L-Lactide *ε*-Caprolactone Poly(L-lactide-*co*-*ε*-caprolactone)

(LL) (CL) P(LL-*co*-CL), PLC

The detail of this study as follow:

1. To study the influence of synthesis scale (25 g, 250 g and 500 g) on the reaction profile in the bulk copolymerization of L-lactide and ε-caprolactone. The effects of the reaction temperature, the reaction time and the monomer to initiator concentration ratio, [M]:[I] on the copolymer properties (% yield, copolymer composition and microstructure, molecular weight, morphology and thermal properties) were investigated.
2. To fabrication of PLC copolymer film and tube by solvent casting, dip-coating and melt extrusion techniques. Moreover, the thermal, mechanical and rheological properties of PLC copolymer were characterized by tensile testing, dynamic mechanical analysis (DMA) and melt rheology measurement. Special attention has been paid to use as absorbable nerve guide.